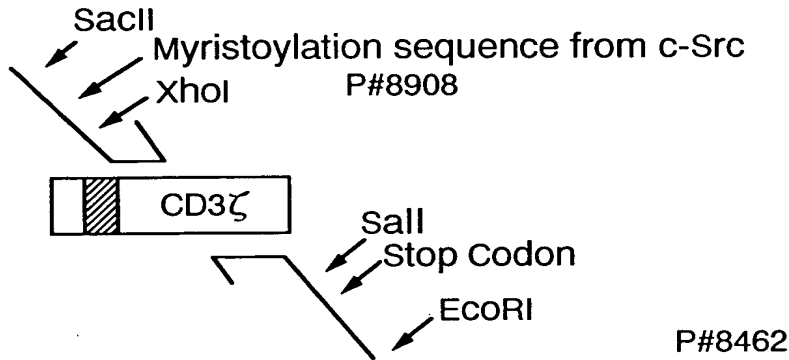


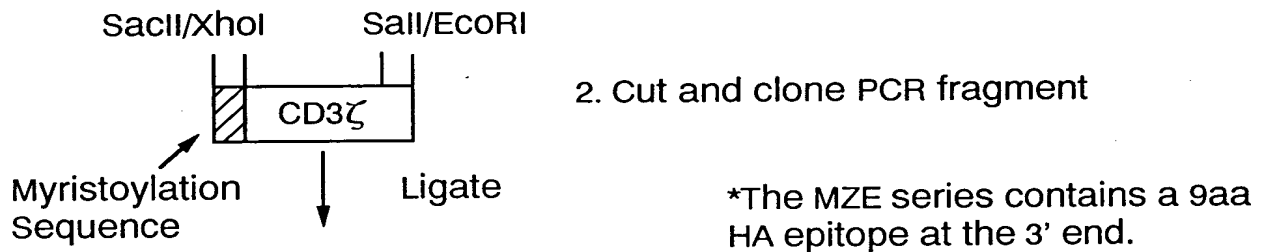
FIG. 1

Construction of intracellular signalling chimera:

1. PCR myristoylated CD3 ζ



2. Cut and clone PCR fragment



3. SEQUENCE insert

4. Cut at XhoI or SalI and add FKBP domains

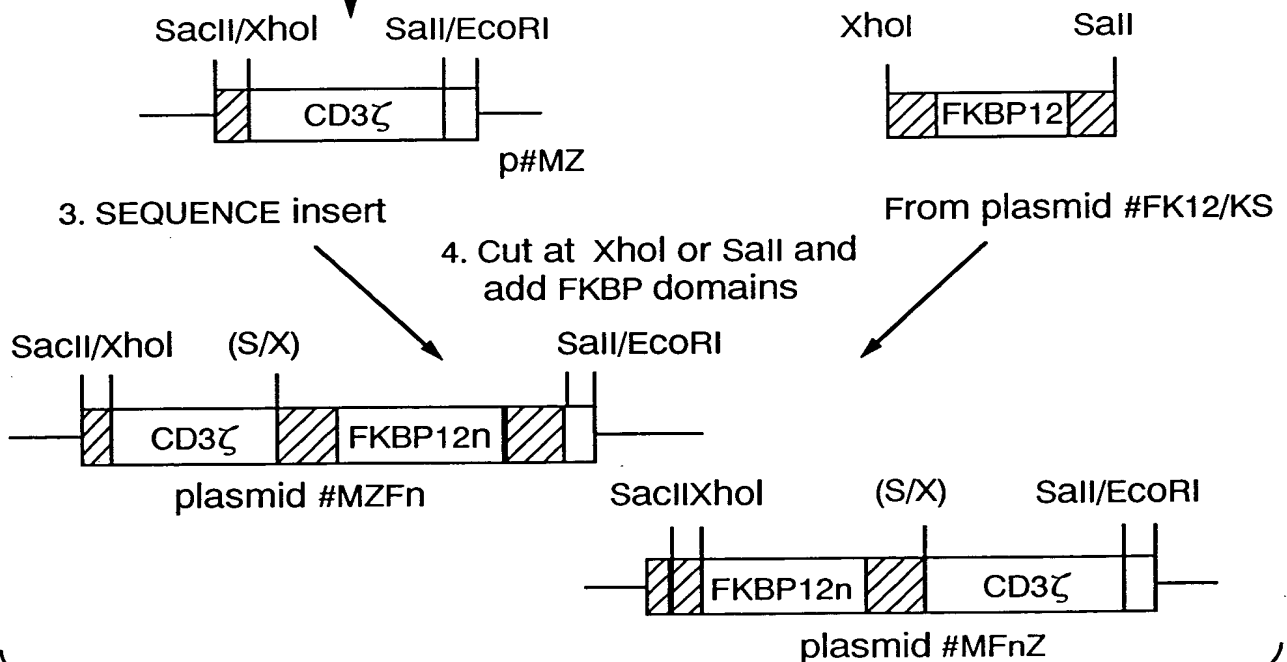
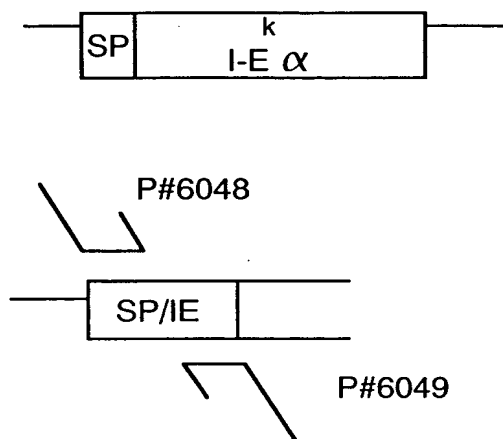


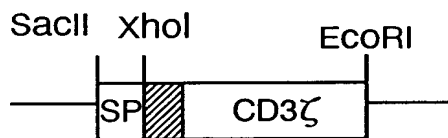
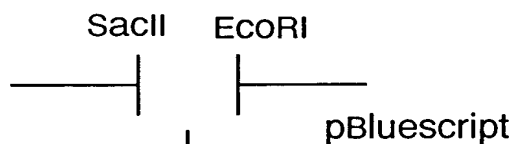
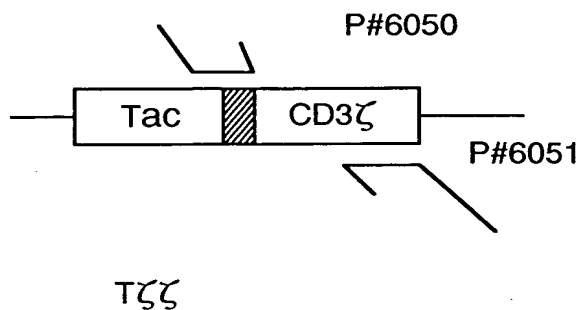
FIG. 2

Construction of extracellular signaling chimera:

1. PCT murine signal peptide



2. PCT CD3 trans-membrane and cytoplasmic domains



plasmid #SPZ/KS
SEQUENCE insert*

Cut XhoI

FIG. 3A

3. PCR FKBP12

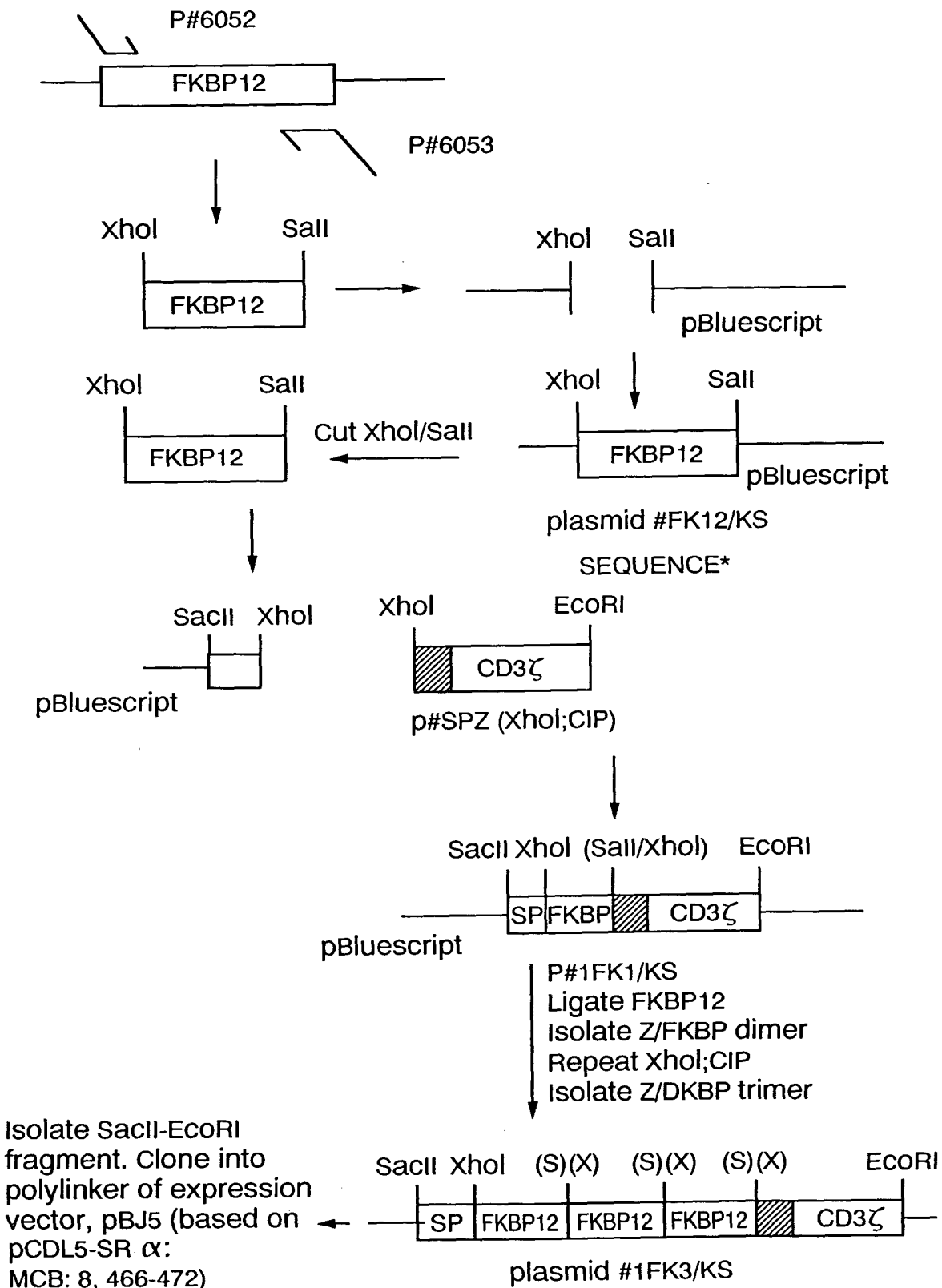


FIG. 3B

五、 在“三反”斗争中，要正确地对待犯错误的干部。对犯错误的干部，不能一棍子打死，要具体分析，区别对待。对于大多数犯错误的干部，要通过教育和帮助，使他们认识错误，改正错误，继续为革命工作。只有极少数严重违法乱纪、屡教不改的干部，才应给予开除公职或刑事处罚。

CYCC

6568: 5' -CGACACTCGAGGTGACGGACAAGGTC-3'

6569: 5' -CGACAGTCGACCCAATCAGGGACCTC-3'




EPITOPE
 7850: 5' - TCGAGTATCC GTACGAC GTACCAGACTACGCAG - 3'
 Y P Y D V P D Y A

7851: 5' - TCGACTGCGTAGTCTGGTACGTCGTACGGATAC - 3' Sall

EPITOPE: 5SEP, 3XEP

8922: 5' - TCGACTATCCGTACGACGTACCAGACTACGCAC - 3'

8923: 5' - TCGAGTGCGTAGTCTGGTACGTCGTACGGATAG - 3'



Myristoylation from c-src 5SMXZ

8908: 5' -CGACACCGCGGCCACCATGGGGAGTAGCAAGAGCAAGCCT
 KOZAK M G S S K S K P

AAGGACCCCAGCCAGCGCCTCGAGAGGAGTGCAGAGACTG-3'
 K D P S Q R L E R S A E T

SacII XhoI ζ -homology

8912: 5' -CGACACTCGAGGAGCTCTGTGACGATG-3'

xhoI homology

E L C D D

FIG. 4B

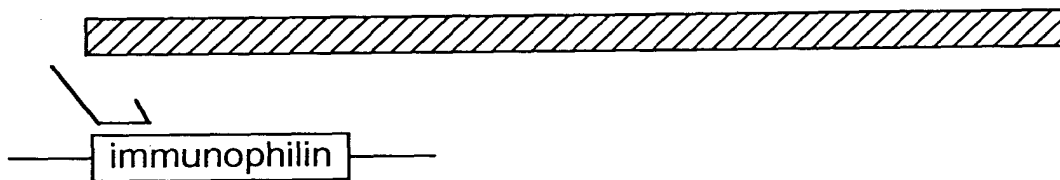
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Asp-Lys #4 XhoI homology
 8061: 5' -CGACACTCGAGCTCTGCTACTTGCTAAAGGGAATCCTCTTC-3'
 E L C Y L L K G I L F

*GATtoAAG

#4 Extension XhoI homology
 8907: 5' -CGACACTCGAGCTGCTGGATCCGAAGCTCTGCTACTTGCTAAAG-3'
 E L L D P K L C Y L L K

TAC-Tm #3 XhoI homology
 7220: 5' -CGACACTCGAGACAACAGAGTACCAGGTAGC-3'
 E T T E Y Q V



FKBP12
 6052: 5' -CGACACTCGAGGGCGTGCAGGTGGAGAC-3'
 E G V Q V E

6053: 5' -CGACAGTCGACTTCCAGTTTTAGAAC-3'
 V E L K L L

FKPB13
 8460: 5' -TCGACACTCGAGACGGGGGCGGAGGGC-3'
 E T G A E G

8461: 5' -CCGACAGTCGACCTCTATTTTGAGCAGC-3'
 V E I

FIG. 4C

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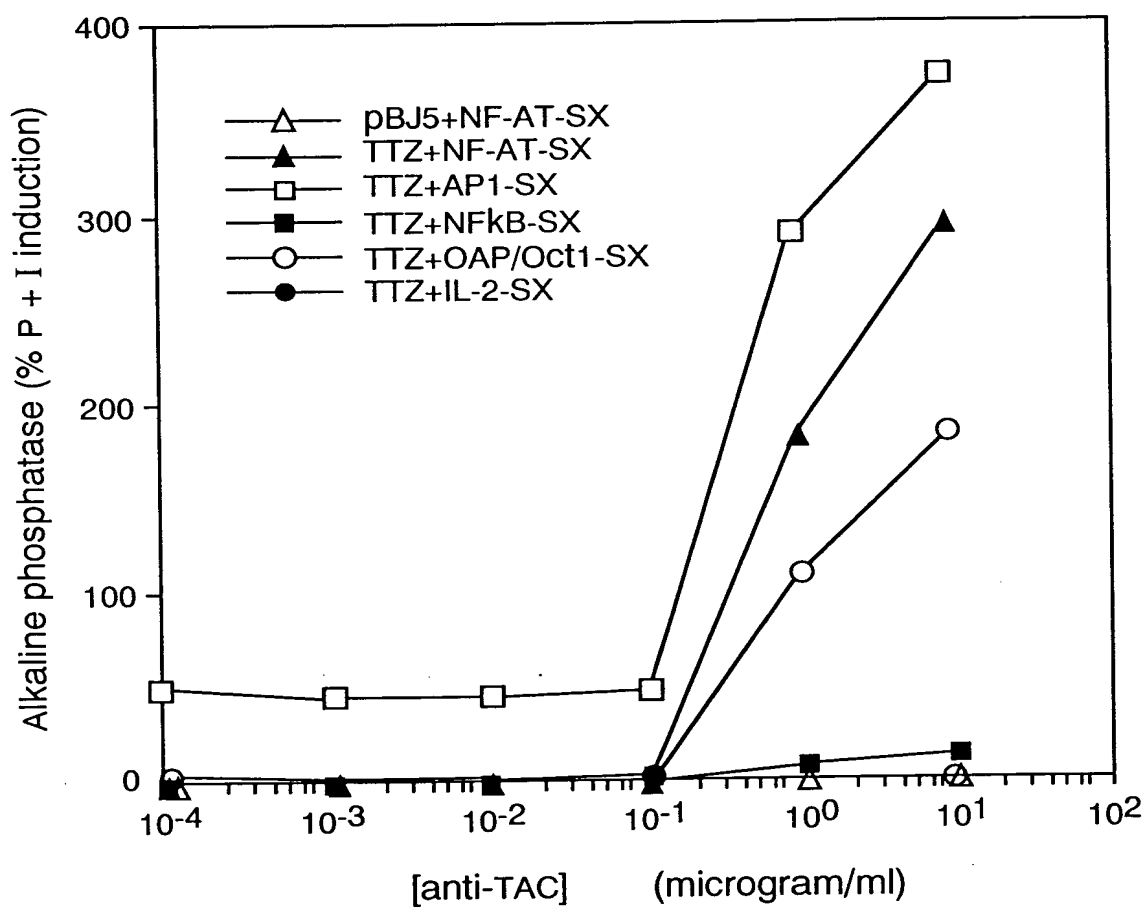


FIG. 5

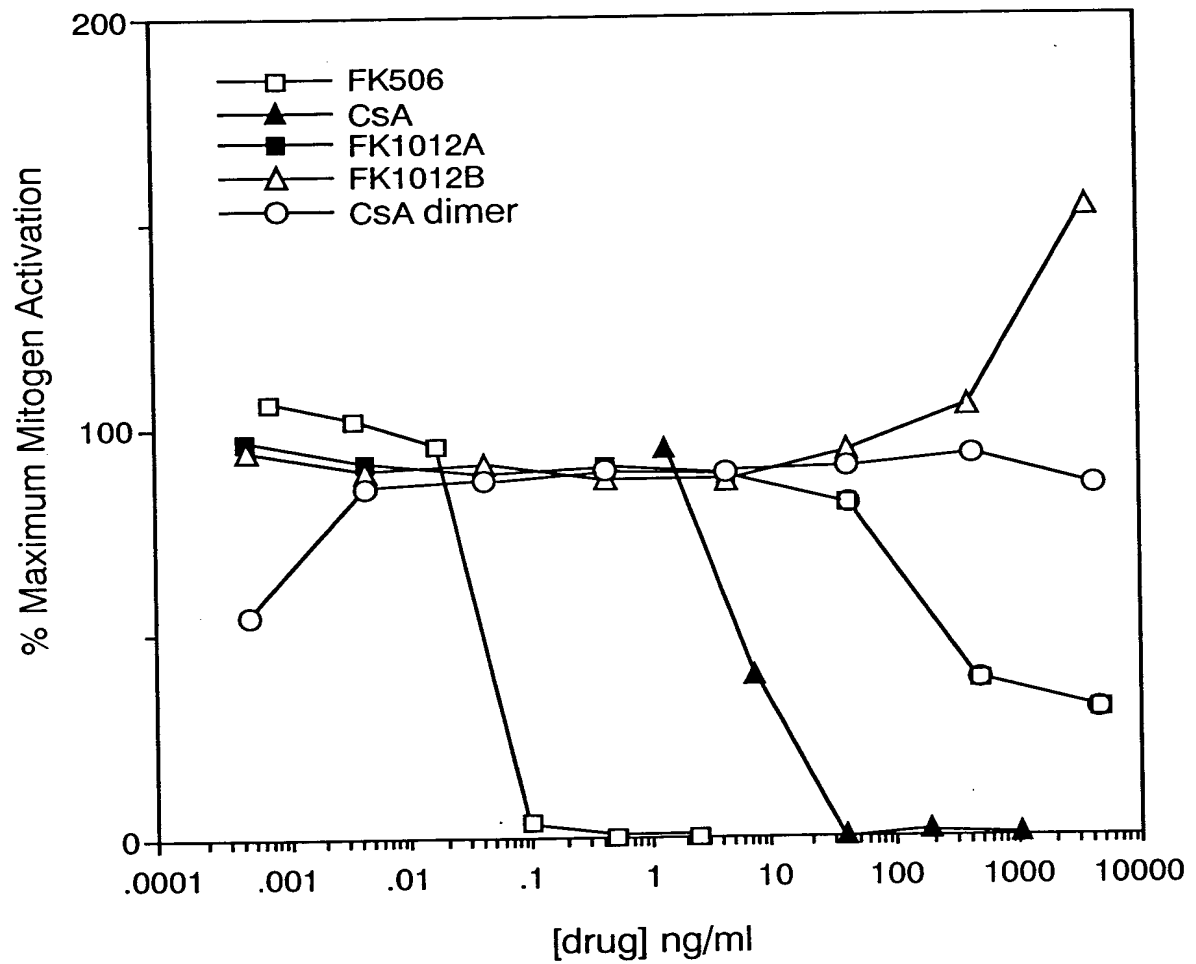
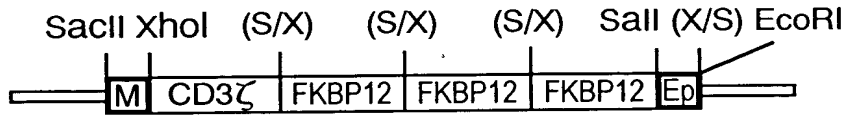
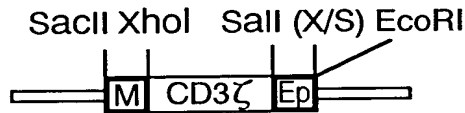


FIG. 6A

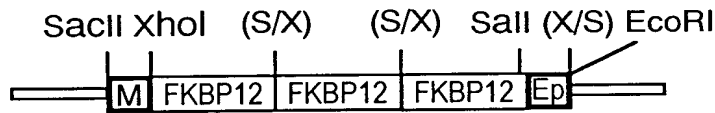


MZF3E

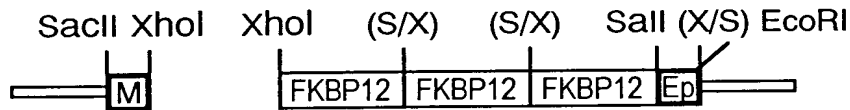


MZE

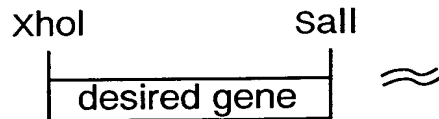
Cut XhoI/SalI; CIP; + FKBP12X3



MF3E



+



1. Cytoplasmic moiety of surface receptor
2. Tyrosine Kinase
3. Transcription Factor
4. Others

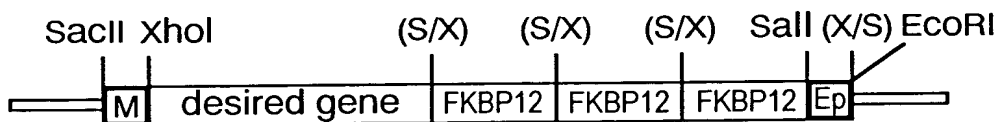


FIG. 6B

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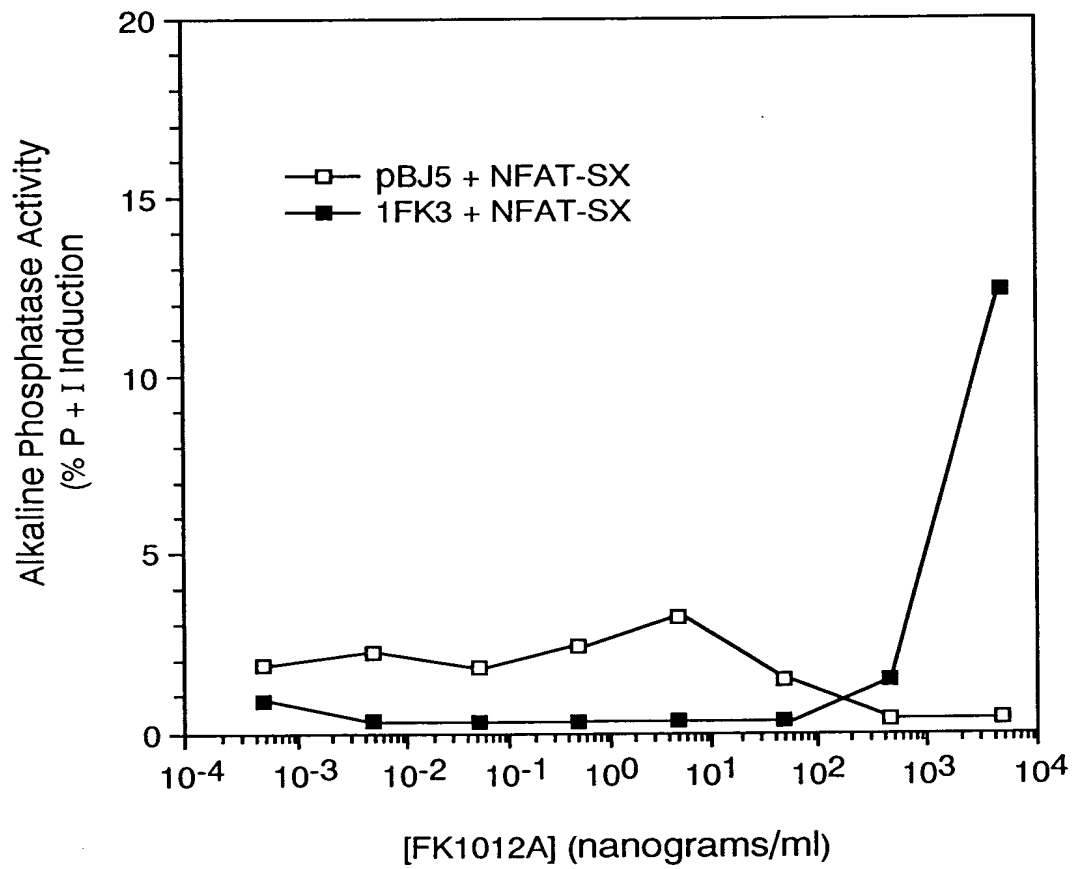


FIG. 7

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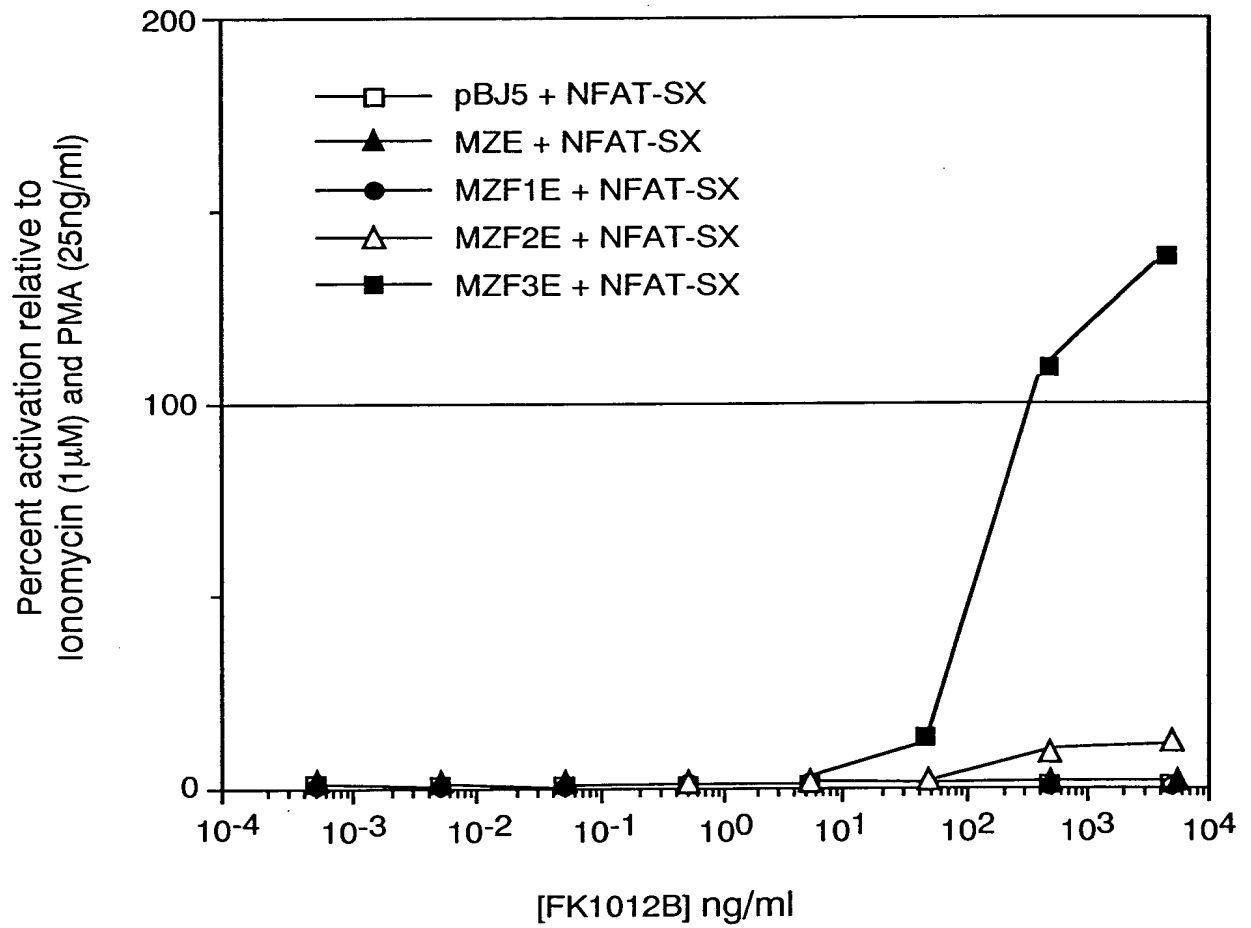


FIG. 8

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00000000000000000000

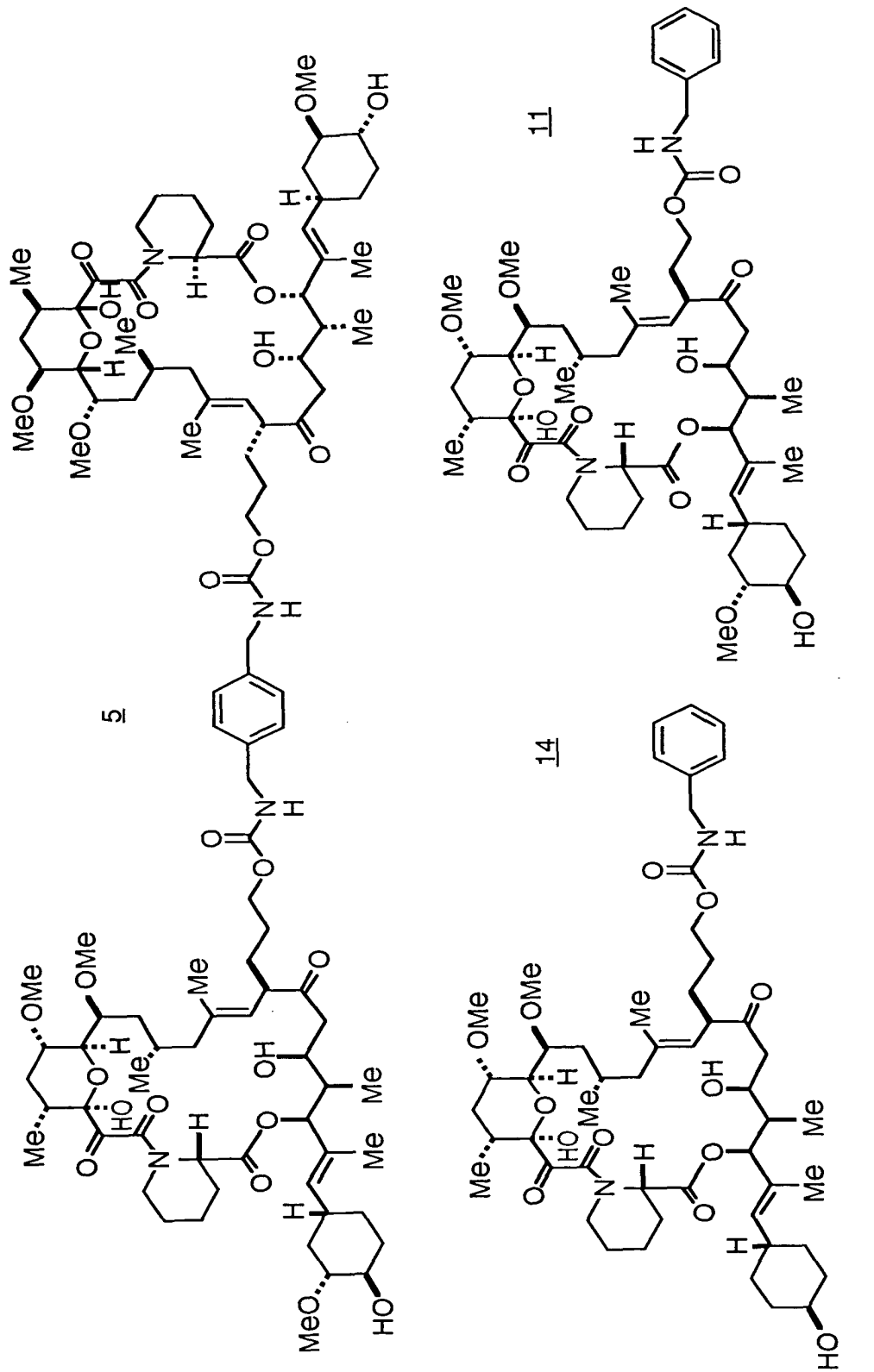
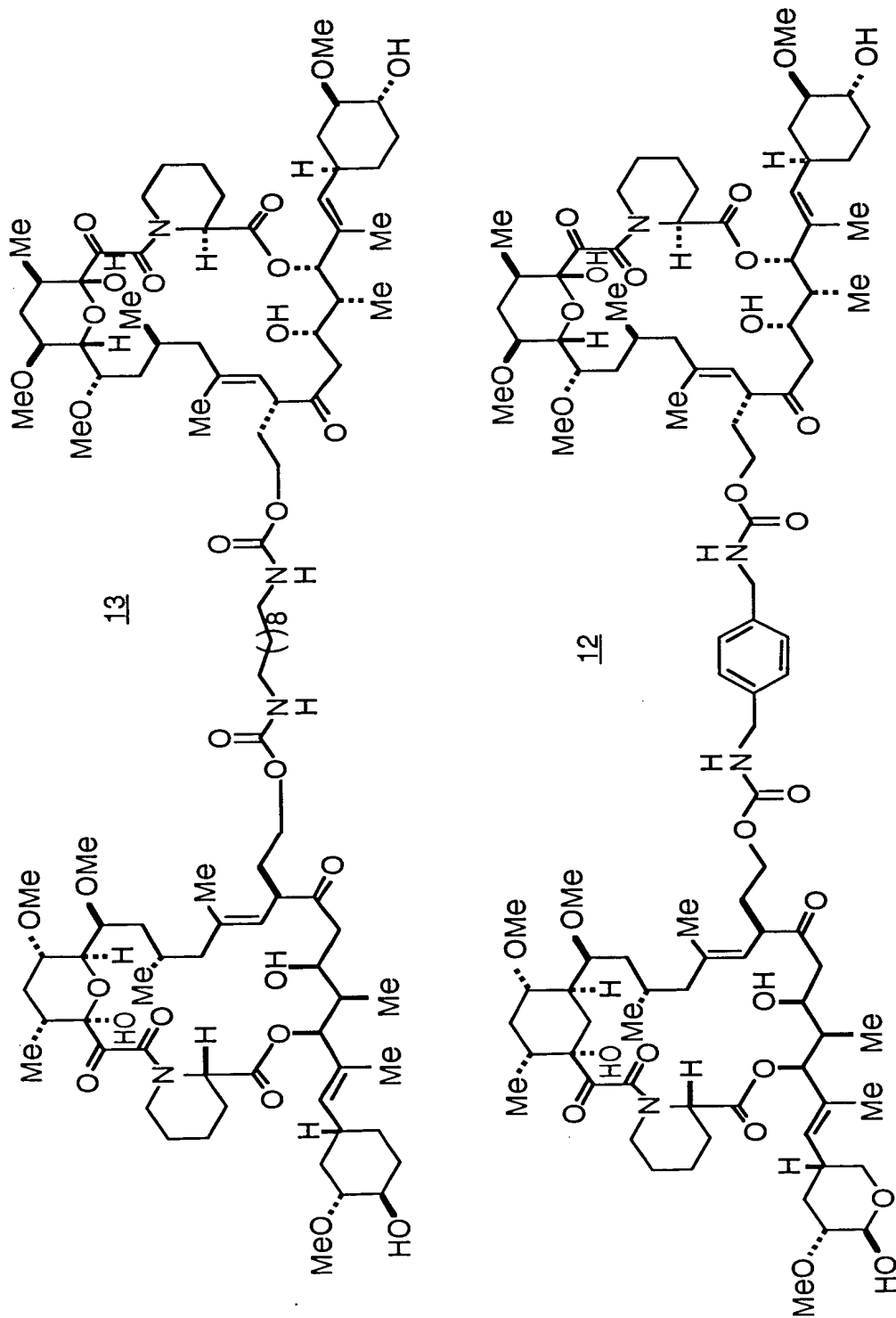
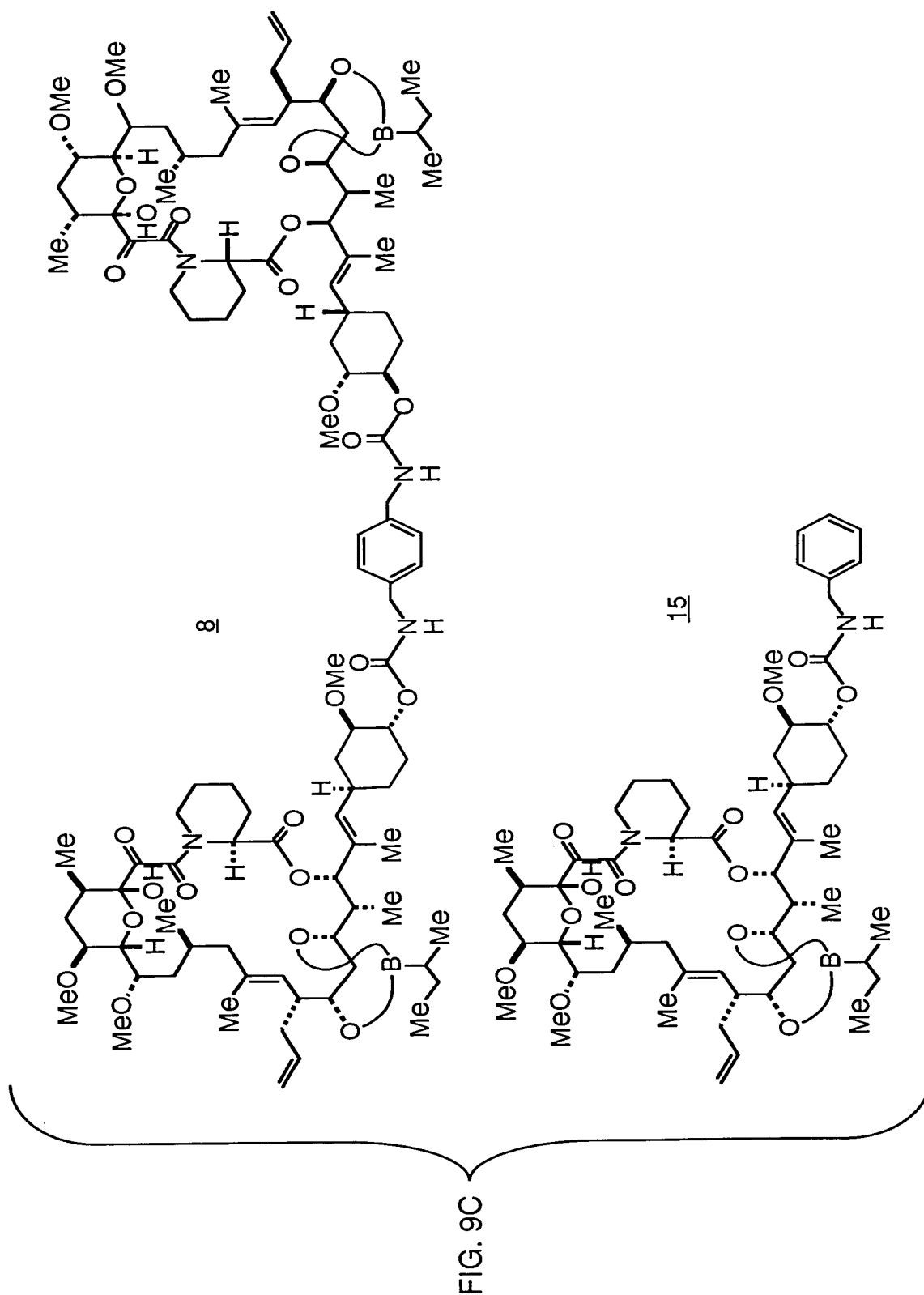


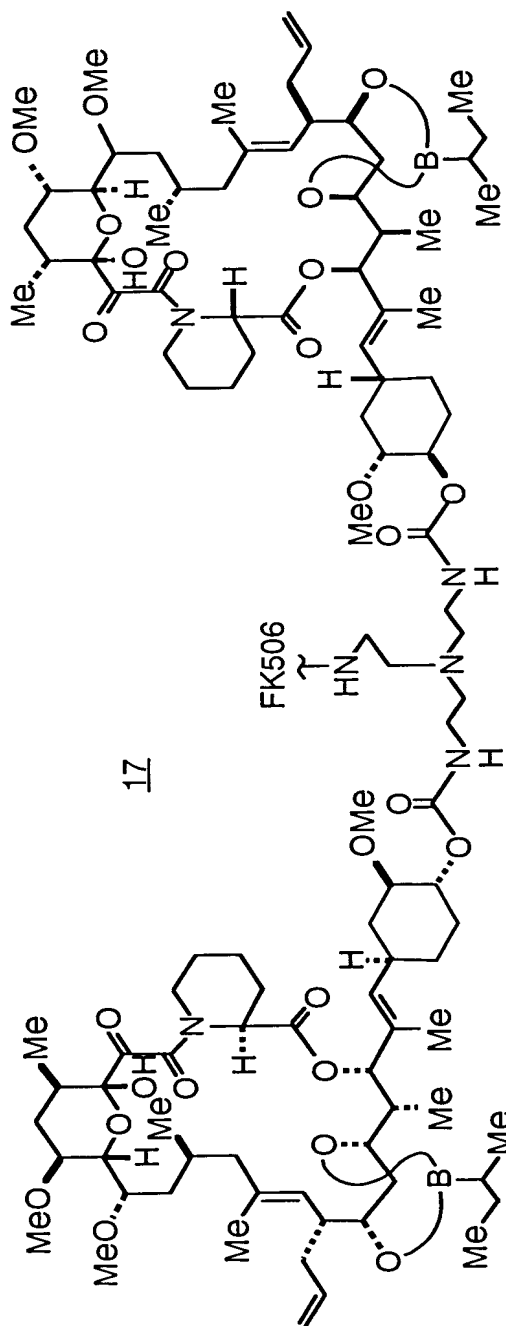
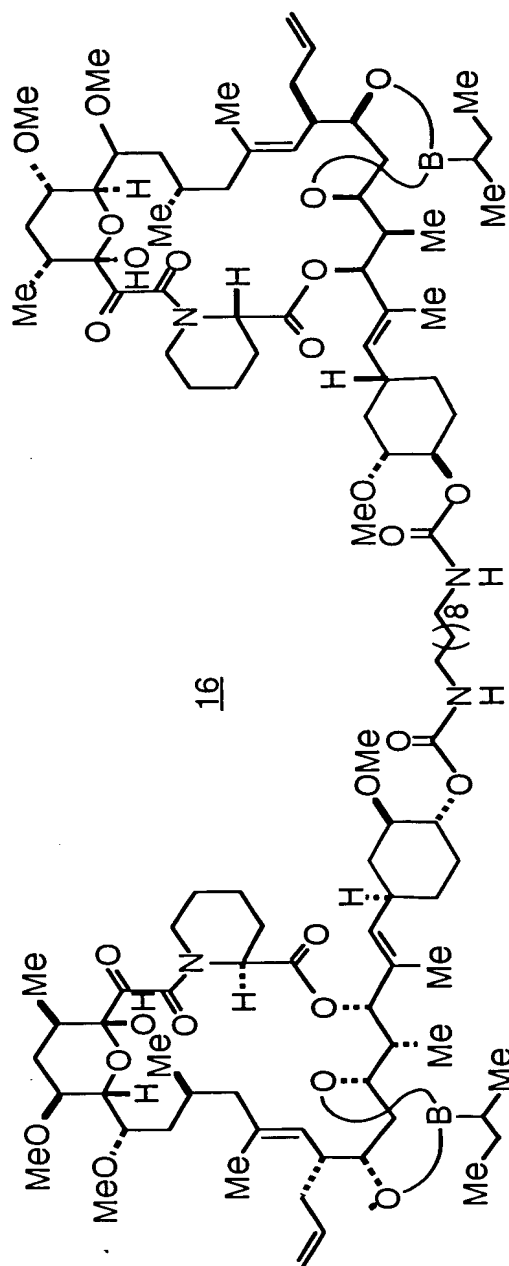
FIG. 9A

FIG. 9B



000000000000000000





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Scheme 1

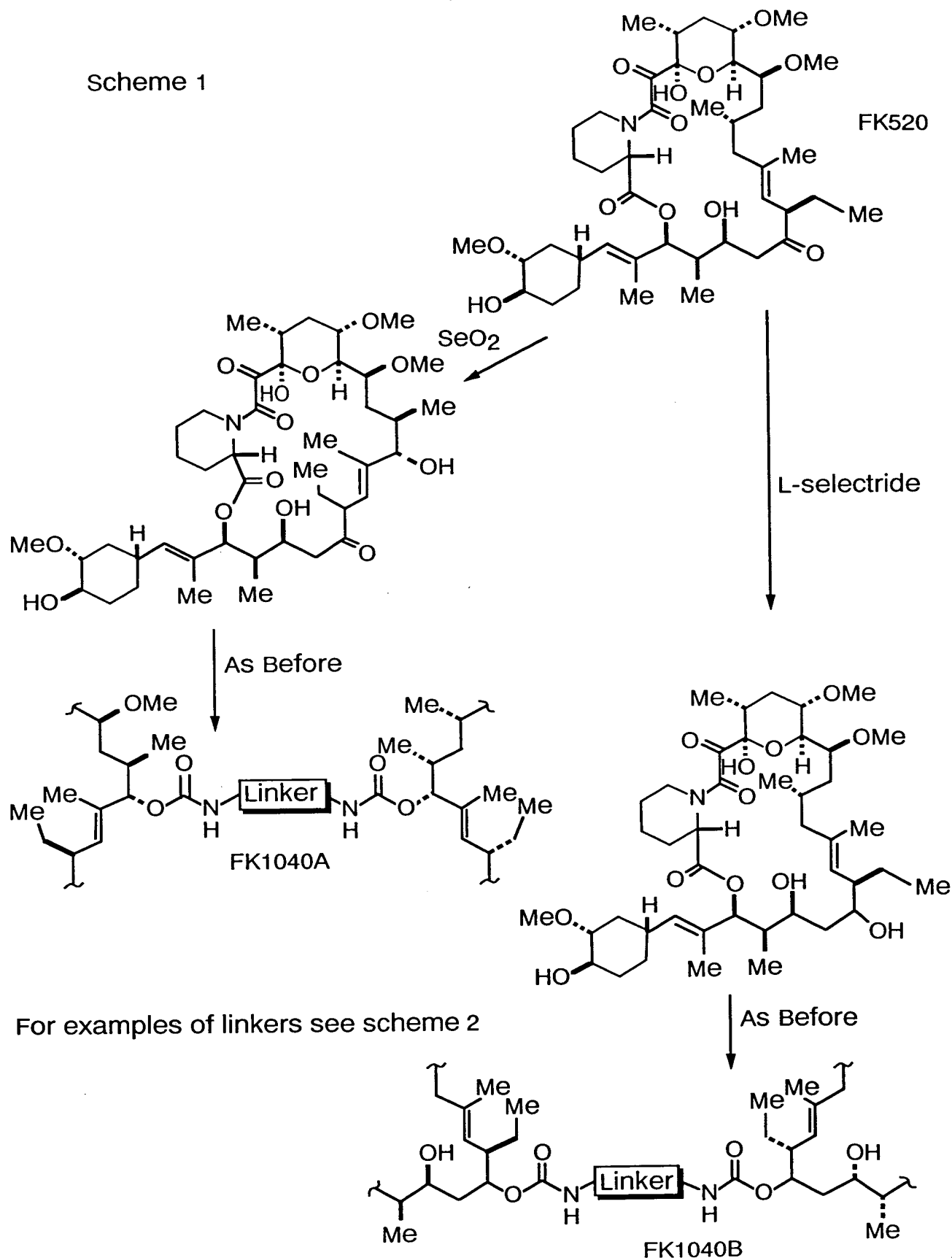


FIG. 10

Scheme 2: Synthesis of Dimers

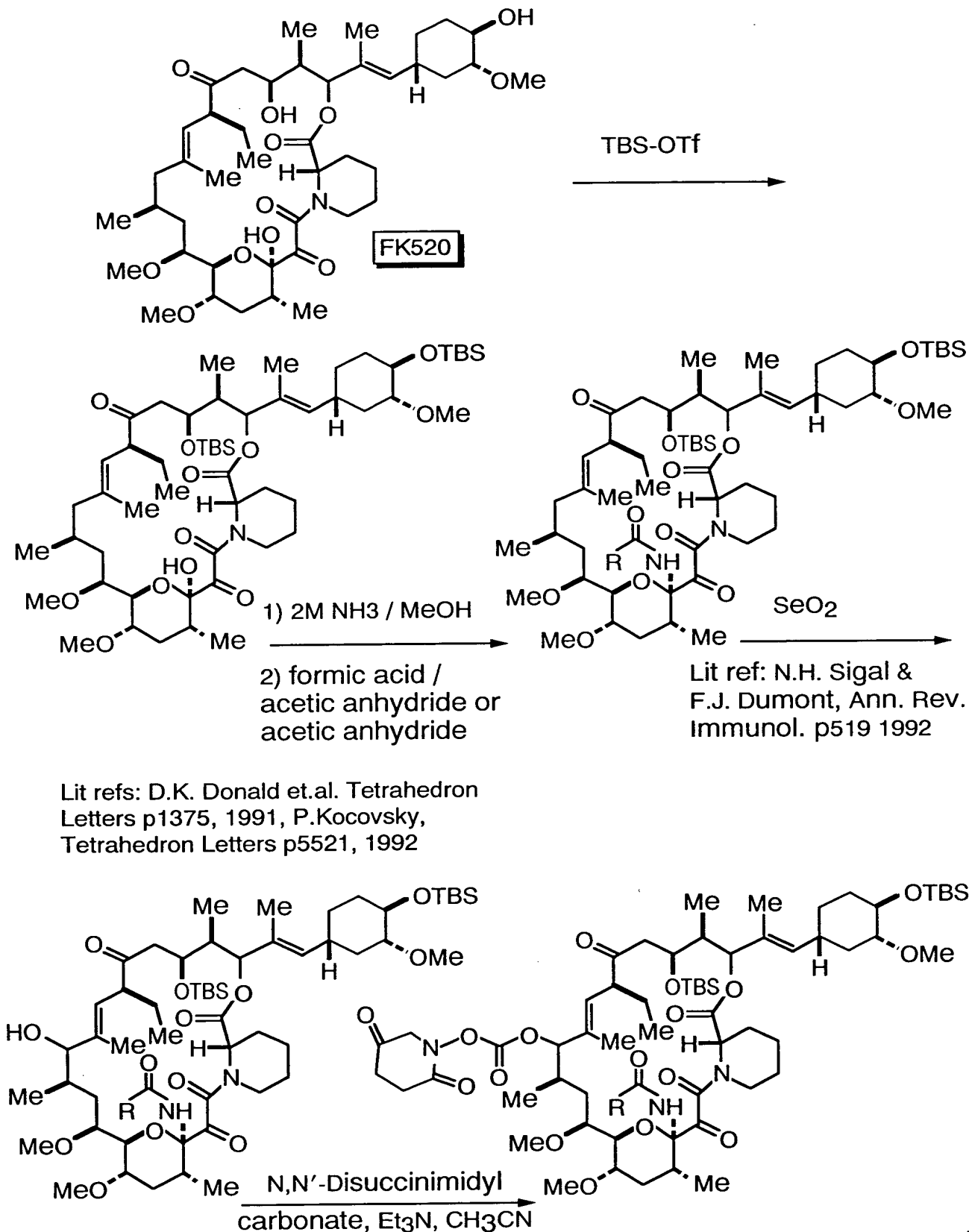


FIG. 11A



FIG. 11B

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

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An additional modified FK520 (FK1040) that interferes with FKBP12 yet should bind the FKBP12 mutant: F36A or F99A or Y26A, or combinations thereof is

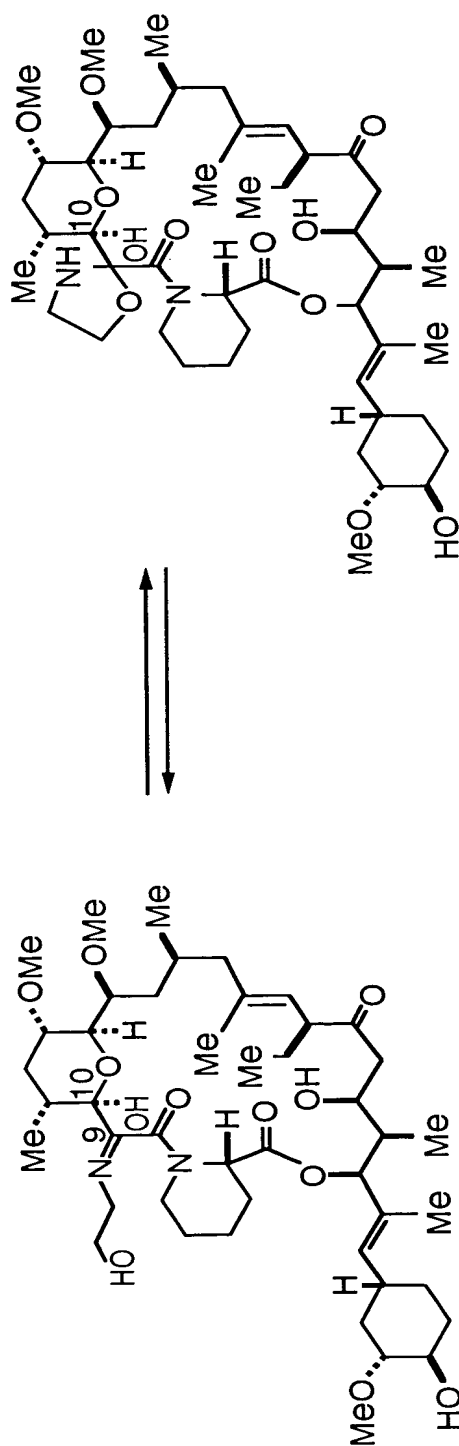


FIG. 11C

Scheme 3 Heterodimerization

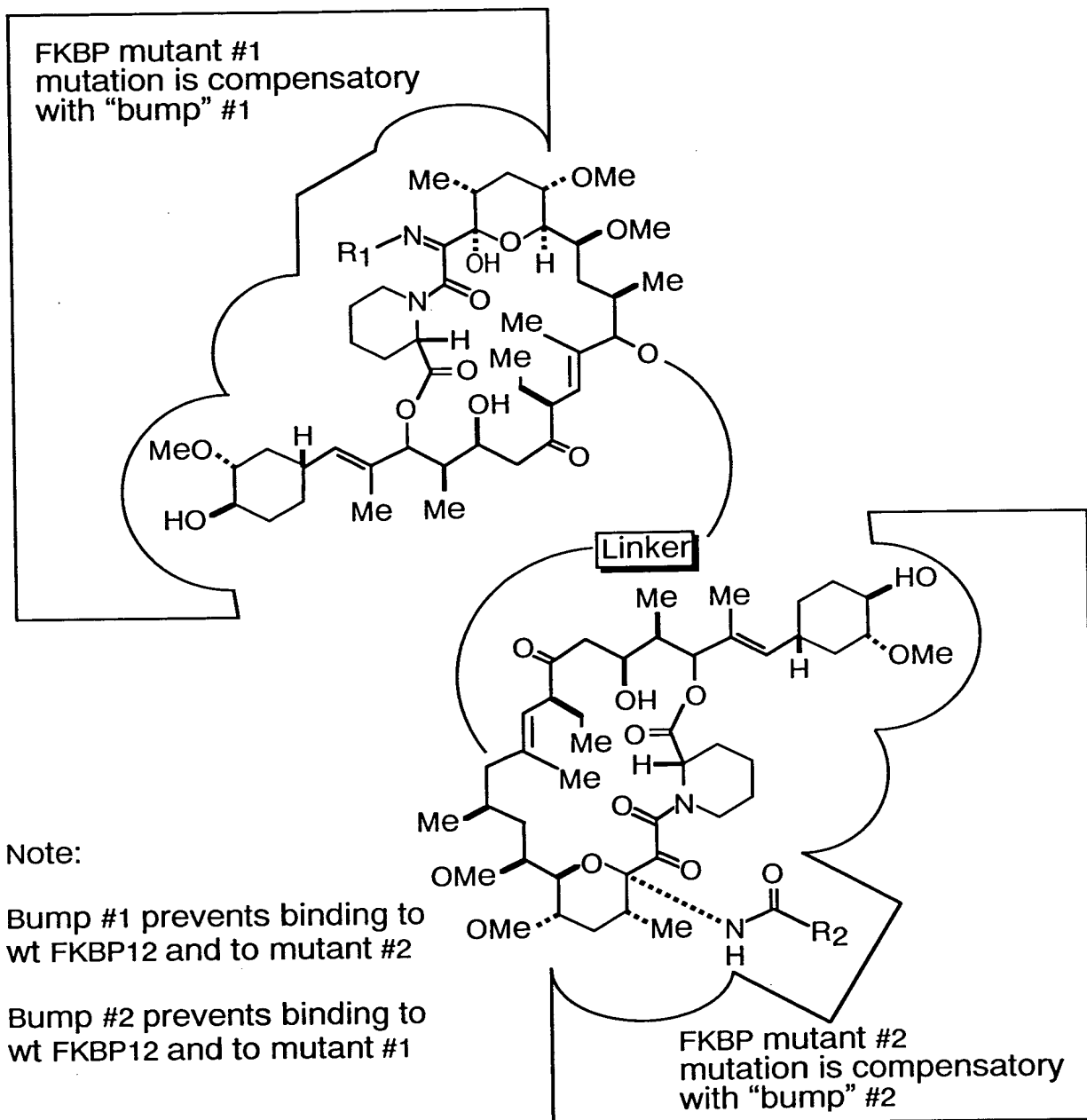
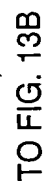
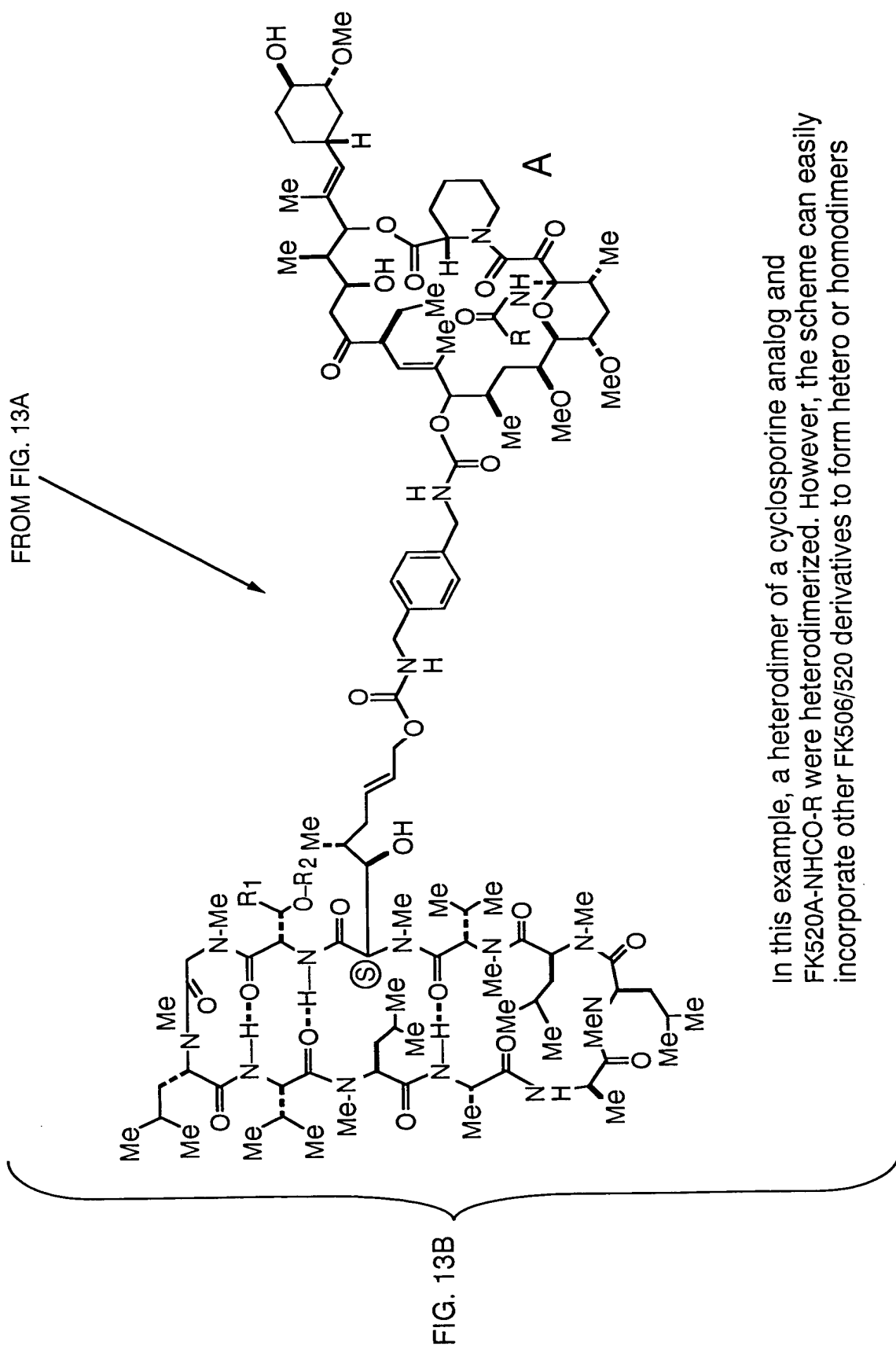


FIG. 12

FIG. 13A





In this example, a heterodimer of a cyclosporine analog and FK520A-NHCO-R were heterodimerized. However, the scheme can easily incorporate other FK506/520 derivatives to form hetero or homodimers

SECRET

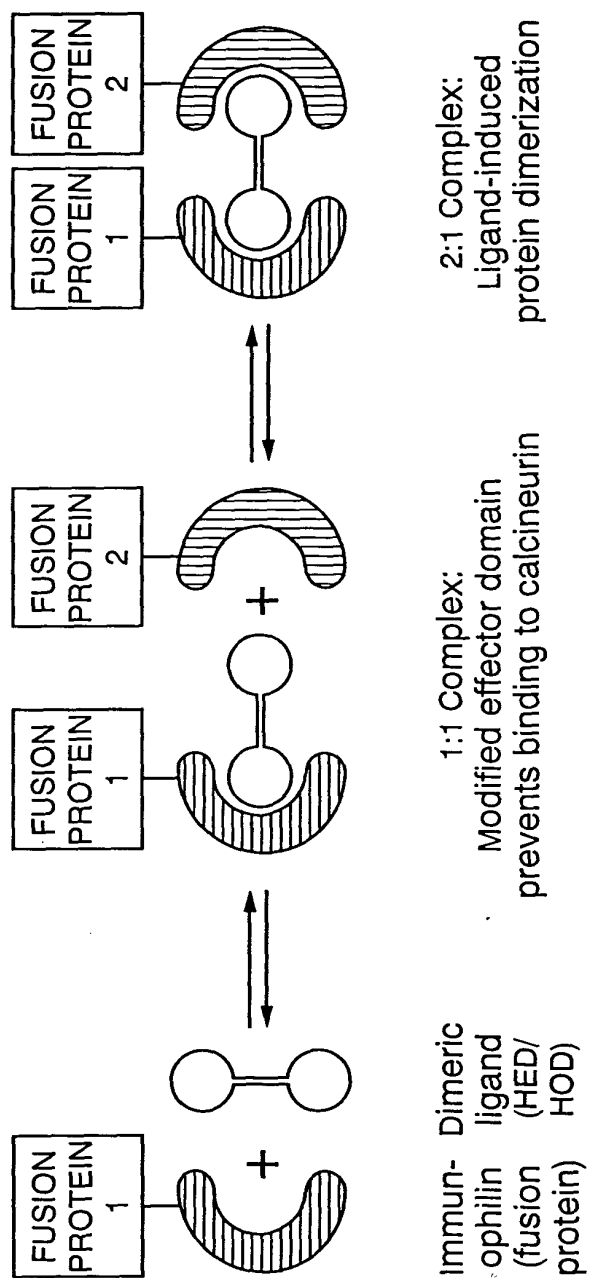


FIG. 14

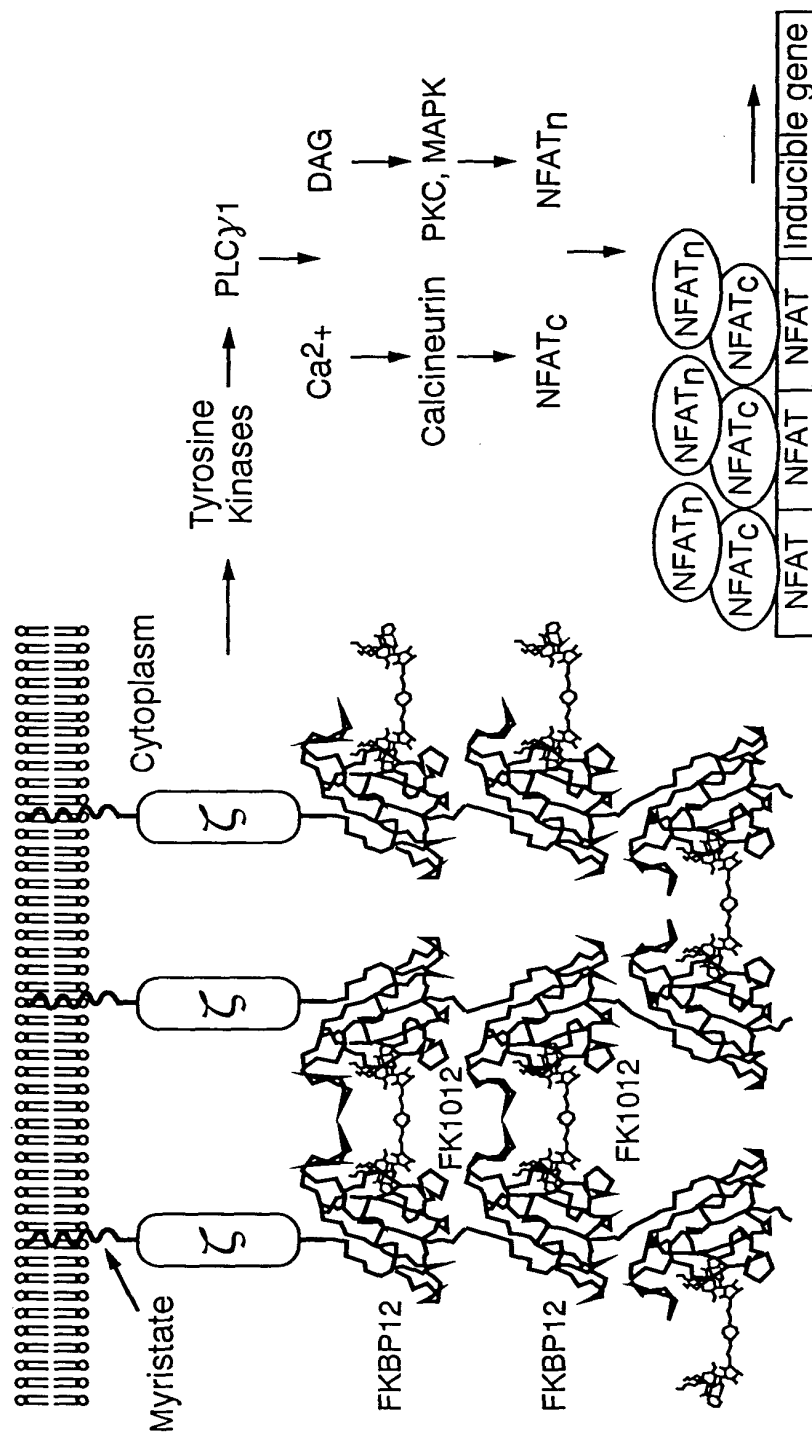


FIG. 15

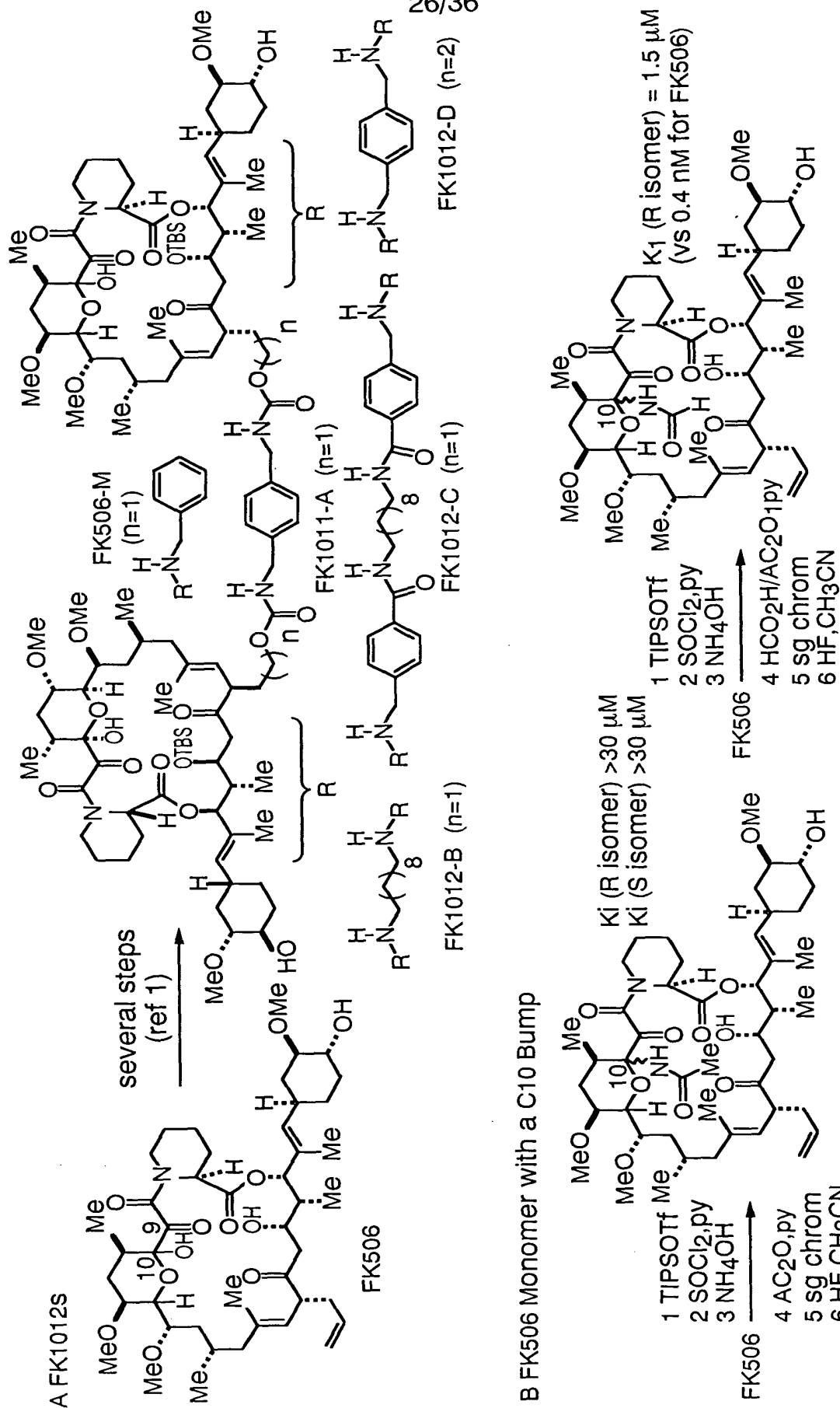
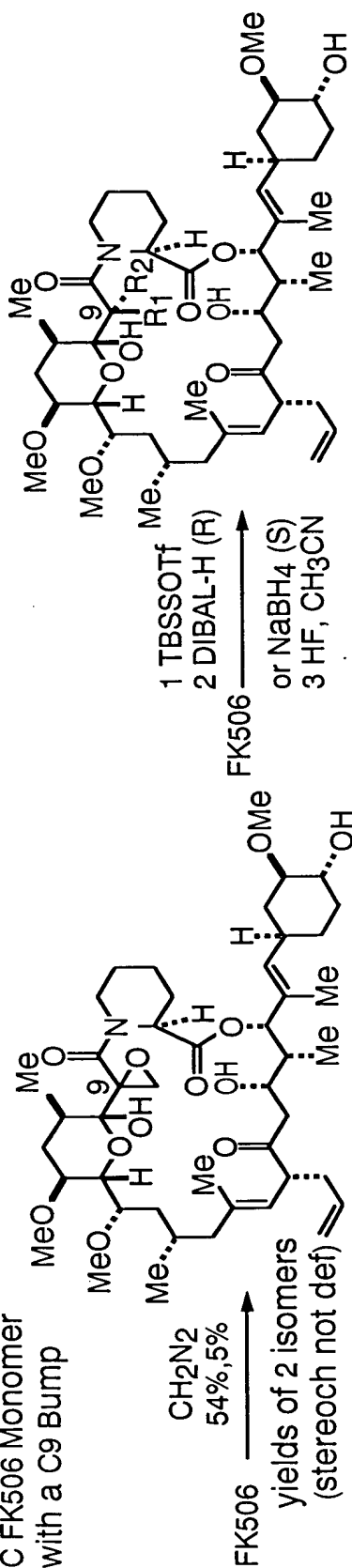


FIG. 16A

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C FK506 Monomer
with a C9 Bump



D HED Reagent Synthesis

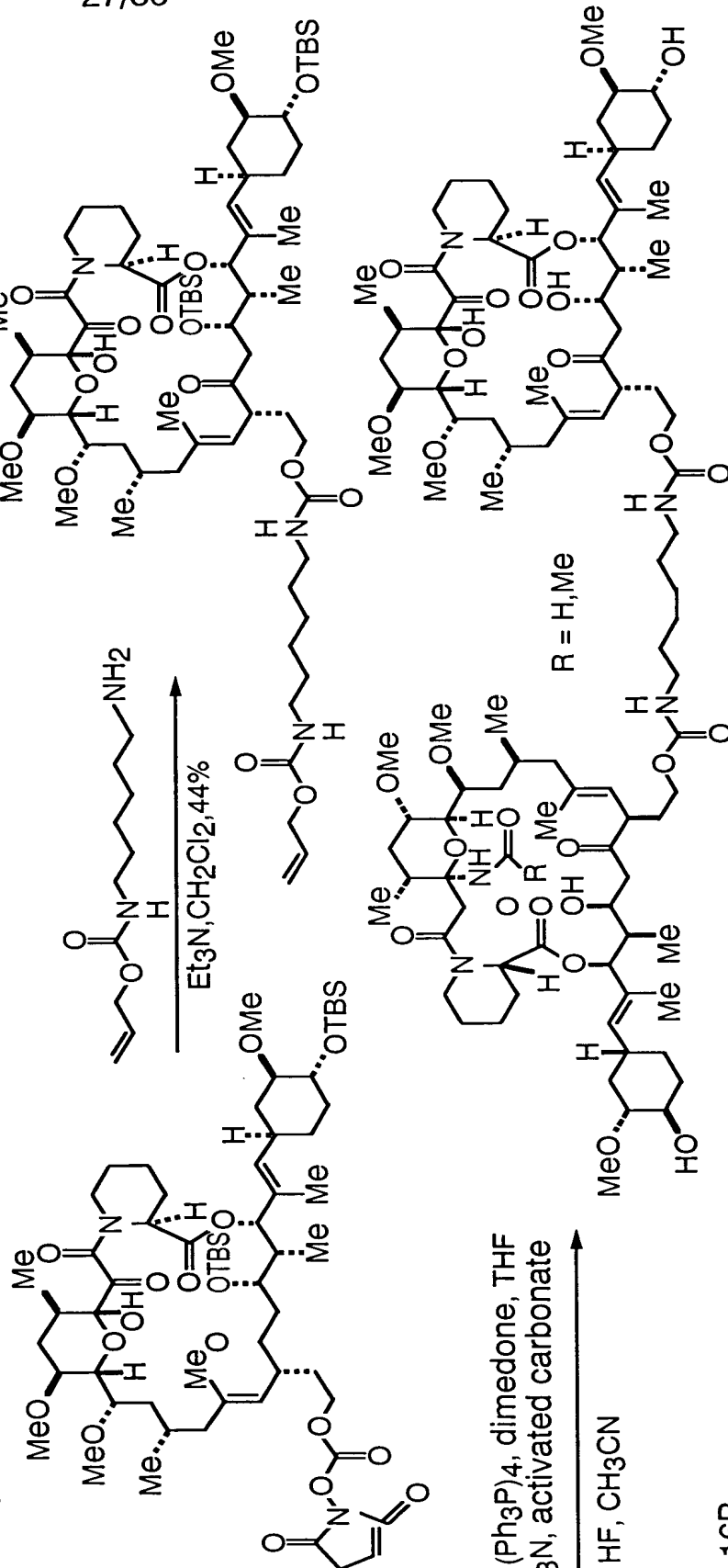


FIG. 16B

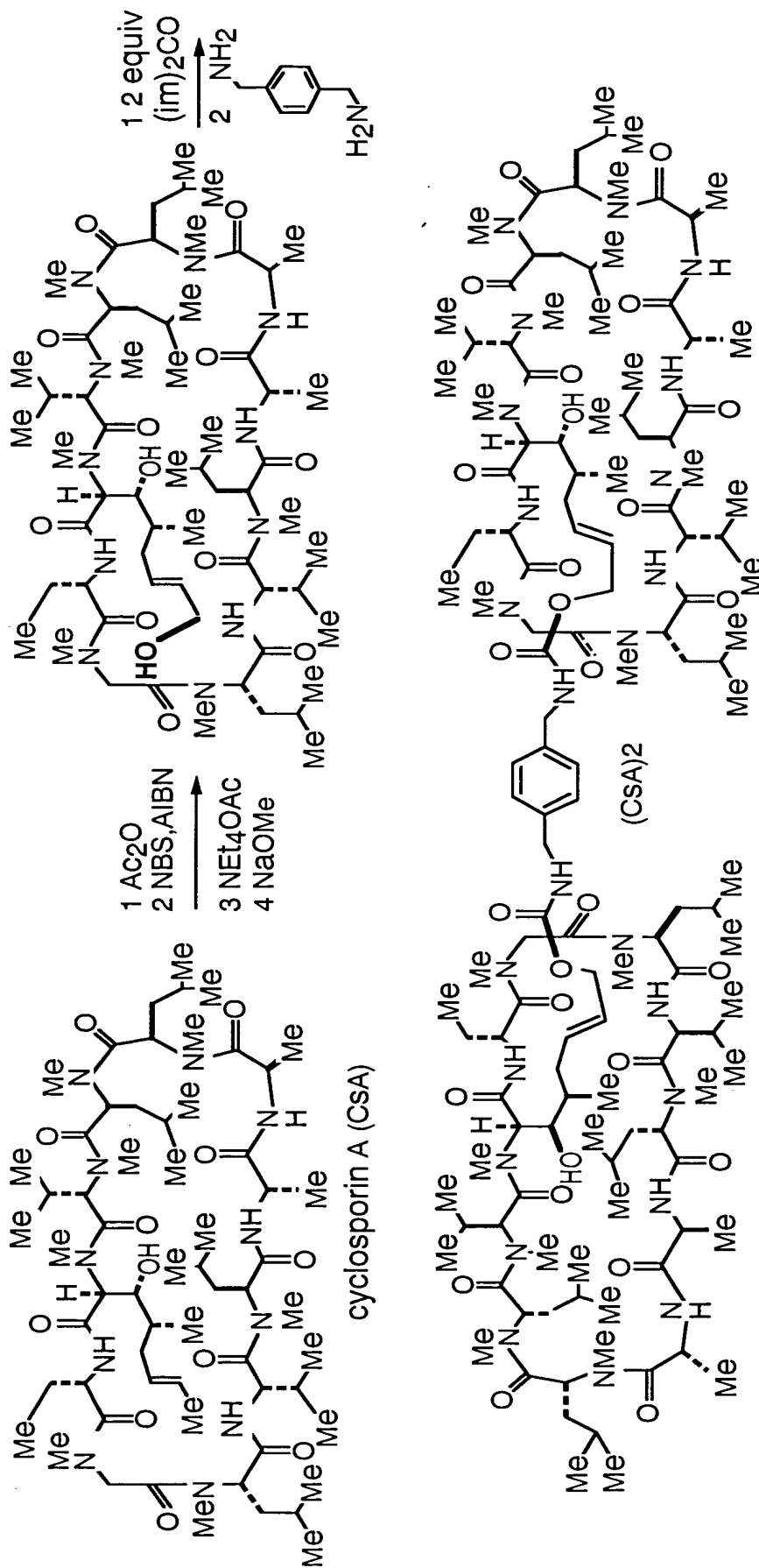


FIG. 17

FIG. 18A

A cDNA construct

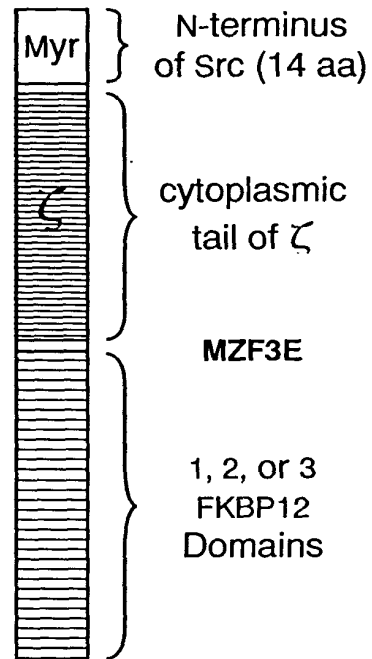
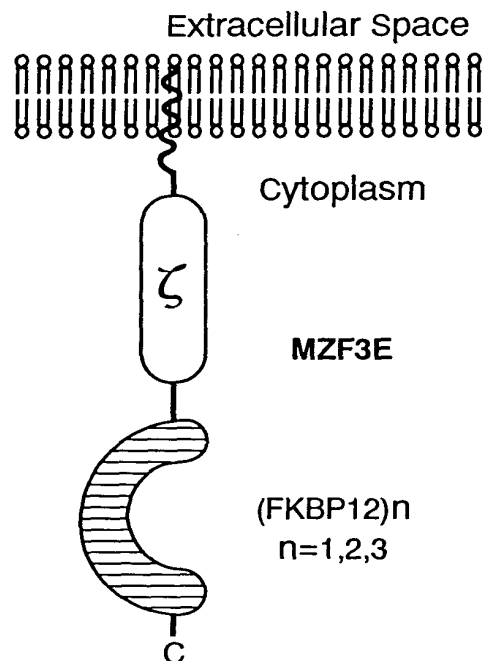


FIG. 18B

B expressed protein



+

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FK1012

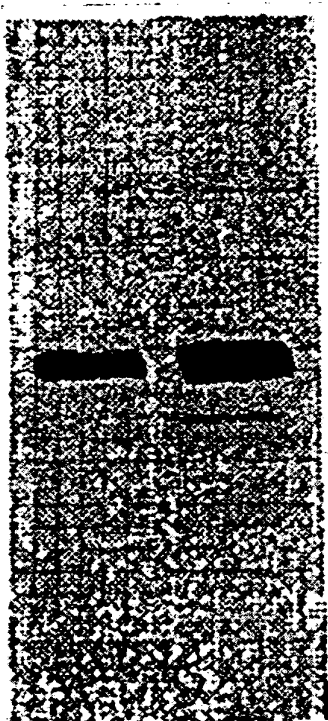
-

+

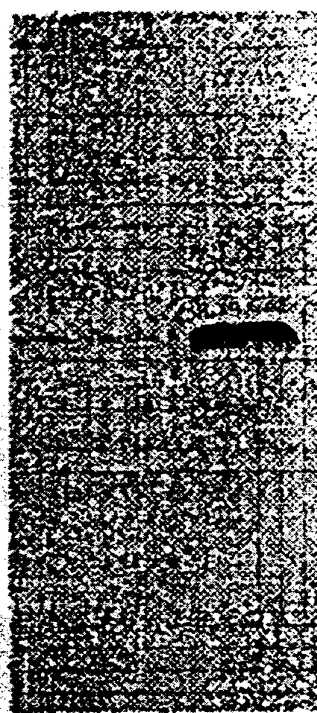
-

+

MZF1E_{f,h} -
(28kDa)



αFlag-blot



αFlu-blot

FIG. 19



FIG. 20

[illegible]

002727-89595160

CLASS	
SUBCLASS	
BY	
DRAFTSMAN	

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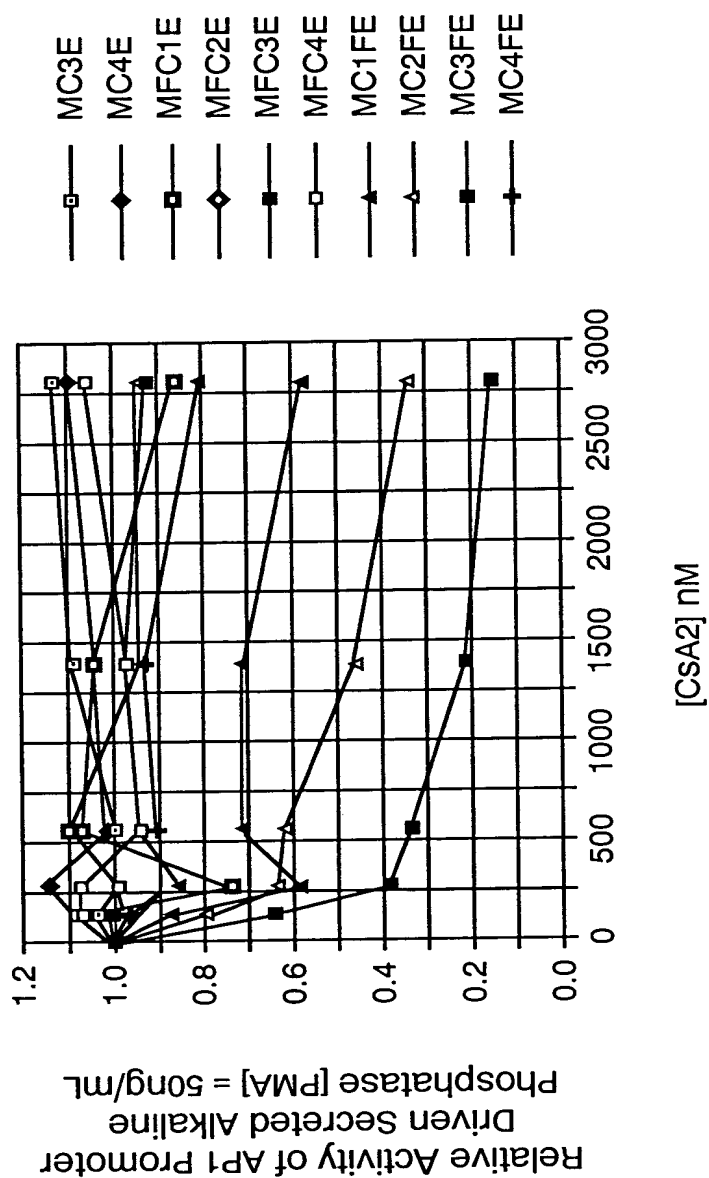


FIG. 21A

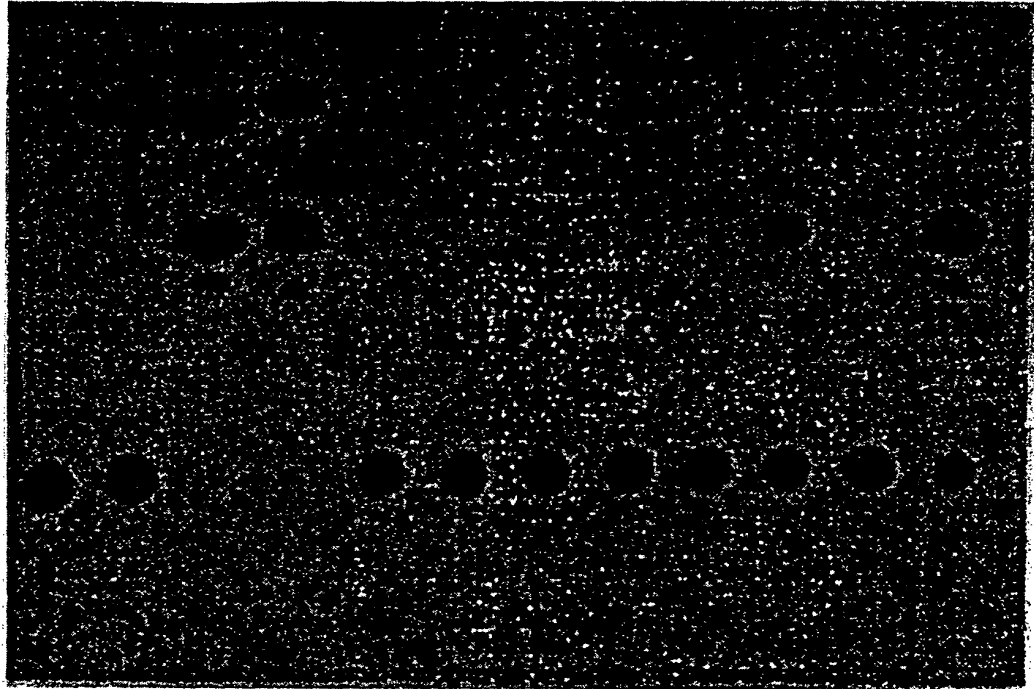
	LD50 Jurkat Cells				Relative Protein Expression
	Myr	Fas	FKBP	FKBP Ep	
A	Myr	Fas	FKBP	FKBP Ep	15nM
MFF3E	Myr	Fas	FKBP	FKBP Ep	+
B	Myr	Fas	CypC	Ep	NA
MFC1E	Myr	Fas	CypC	Ep	-
MFC2E	Myr	Fas	CypC	Ep	-
MFC3E	Myr	Fas	CypC	Ep	-
MFC4E	Myr	Fas	CypC	Ep	-
MC1FE	Myr	CypC	Fas	Ep	500nM
MC2FE	Myr	CypC	Fas	Ep	300nM
MC3FE	Myr	CypC	CypC	Ep	200nM
MC4FE	Myr	CypC	CypC	Fas Ep	+/-
MC3E	Myr	CypC	CypC	Ep	+++
MC4E	Myr	CypC	CypC	Ep	+++

FIG. 21B

+

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00222 00551100



•	•	•	•	•	•	•	•	•	•	•	•
-	+	-	+	-	+	-	+	-	+	-	+
1		2		3		4		5		6	

FIG. 22

+

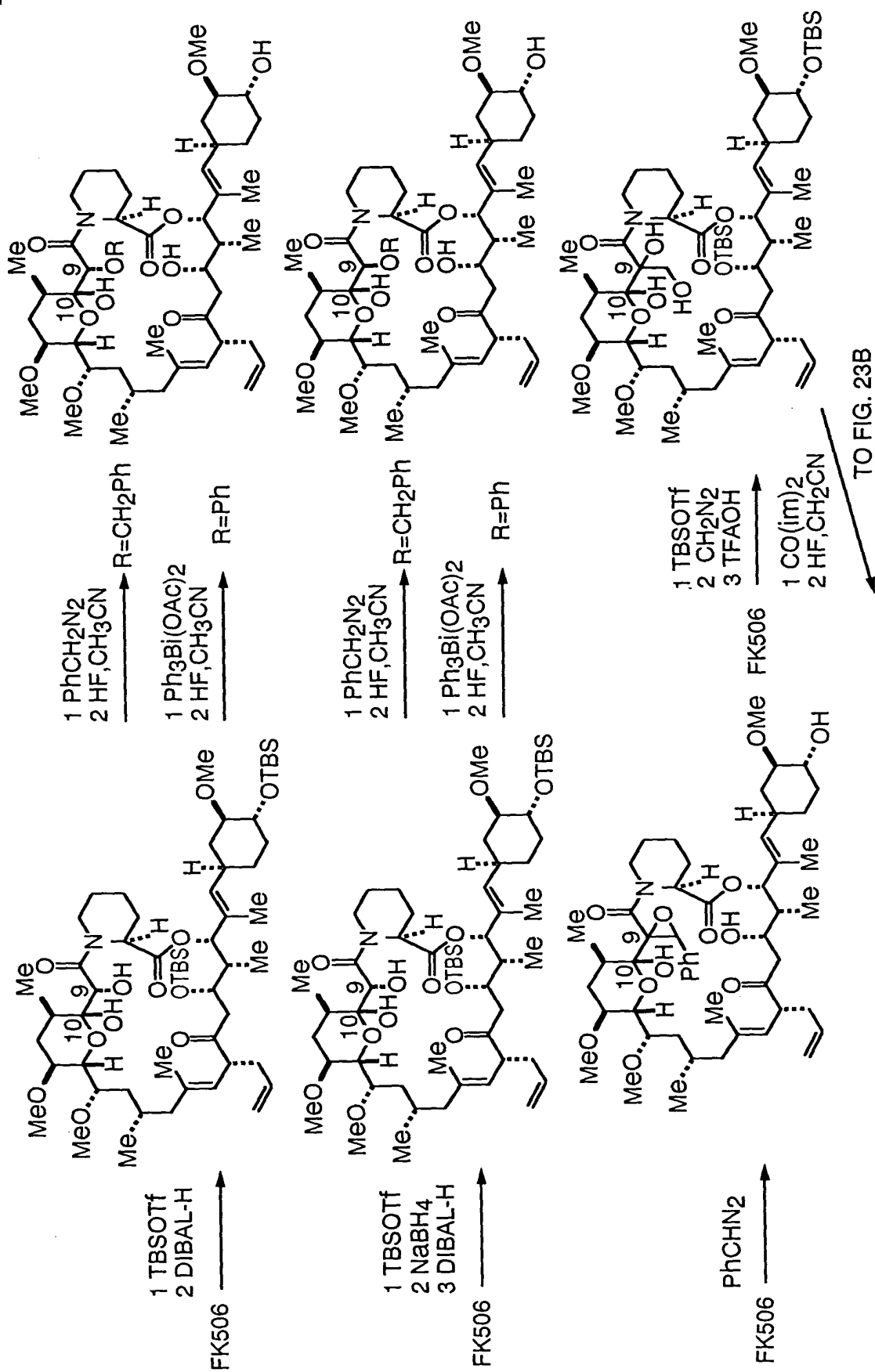


FIG. 23A

TO FIG. 23B

0027-8553760

